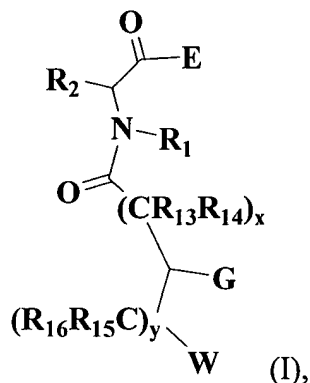


## Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of claims:

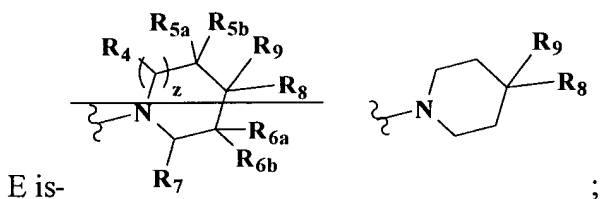
- (Currently amended) A compound of formula (I),



or a pharmaceutically-acceptable salt or hydrate, thereof, in which:

R<sub>1</sub> is hydrogen or C<sub>1-6</sub>alkyl or is taken together with R<sub>2</sub> or R<sub>3</sub> to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;

R<sub>2</sub> is C<sub>1-6</sub>alkyl or C<sub>2-6</sub>alkenyl optionally substituted with one to three-aryl, cycloalkyl, or heteroaryl, provided that where G is C<sub>2-6</sub>alkenyl, A<sub>1</sub>-NR<sub>18</sub>CO<sub>2</sub>R<sub>19</sub>, or A<sub>1</sub>-SO<sub>2</sub>R<sub>17</sub>, or when y is 0, R<sub>2</sub> may be or C<sub>1-6</sub>alkyl or C<sub>2-6</sub>alkenyl, each optionally substituted with heteroaryl;



G is selected from A<sub>3</sub>-aryl, ~~OR<sub>18</sub>, heteroaryl, A<sub>1</sub>-cyano, A<sub>2</sub>-OR<sub>17</sub>, A<sub>4</sub>-C(=O)R<sub>18</sub>, A<sub>4</sub>-CO<sub>2</sub>R<sub>18</sub>,  
A<sub>4</sub>-C(=O)NR<sub>18</sub>R<sub>19</sub>, A<sub>4</sub>-OC(=O)R<sub>18</sub>, A<sub>1</sub>-NR<sub>18</sub>C(=O)R<sub>19</sub>, A<sub>4</sub>-OC(=O)NR<sub>18</sub>R<sub>19</sub>,  
A<sub>1</sub>-NR<sub>18</sub>SO<sub>2</sub>R<sub>17</sub>, A<sub>1</sub>-NR<sub>18</sub>CO<sub>2</sub>R<sub>19</sub>, and A<sub>1</sub>-NR<sub>20</sub>C(=O)NR<sub>18</sub>R<sub>19</sub>, and A<sub>4</sub>-SR<sub>18</sub>; or when y is~~

~~0, or when W is a group other than NHR<sub>22</sub>, G may be A<sub>4</sub>-heterocyclo, wherein A<sub>4</sub> is a bond,~~

~~C<sub>1-6</sub>alkylene or C<sub>2-6</sub>alkenylene (straight or branched chain), A<sub>2</sub> is C<sub>1-6</sub>alkylene or C<sub>2-</sub>~~

~~6alkenylene, and A<sub>3</sub> is C<sub>2-6</sub>alkenylene; or where G is C<sub>2-6</sub>alkenyl, A<sub>1</sub>-NR<sub>18</sub>CO<sub>2</sub>R<sub>19</sub>, or~~

~~A<sub>4</sub>-SO<sub>2</sub>R<sub>17</sub>, or when y is 0, R<sub>2</sub> may be C<sub>1-6</sub>alkyl or C<sub>2-6</sub>alkenyl, each substituted with~~

~~heteroaryl;~~

~~heteroaryl;~~

W is selected from ~~NR<sub>21</sub>R<sub>22</sub>, OR<sub>23</sub>, NR<sub>24</sub>C(=O)R<sub>24</sub>, NR<sub>24</sub>CO<sub>2</sub>R<sub>24</sub>, amidino, guanidino, or a substituted or unsubstituted heterocyclo, heteroaryl, or cycloalkyl selected from azepinyl, azetidiny, and imidazolyl, imidazolidinyl, pyrazolyl, pyridyl, pyrazinyl, pyridazinyl, 1,2-dihydropyridazinyl, pyranyl, tetrahydropyranyl, piperazinyl, homopiperazinyl, pyrrolyl, pyrrolidinyl, piperidinyl, thiazolyl, tetrahydrothiazolyl, thienyl, furyl, tetrahydrofuryl, morpholinyl, isoquinolinyl, tetrahydroisoquinolinyl, tetrazolyl, oxazolyl, tetrahydro-oxazolyl, and C<sub>3-7</sub>cycloalkyl~~, wherein said heteroaryl, heterocyclo or cycloalkyl groups may additionally have joined thereto an optionally substituted five-to-seven membered heterocyclic, heteroaryl, or carbocyclic ring;

~~R<sub>4</sub> and R<sub>7</sub> are independently selected from hydrogen, alkyl, substituted alkyl, halogen, hydroxy, alkoxy, and keto;~~

~~R<sub>4</sub> R<sub>5</sub>, R<sub>5a</sub>, R<sub>5b</sub>, R<sub>6</sub>, R<sub>6a</sub>, R<sub>6b</sub>, R<sub>8</sub> and R<sub>9</sub> are independently hydrogen, halogen, cyano, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclo, aryl, heteroaryl, OR<sub>25</sub>, NR<sub>25</sub>R<sub>26</sub>, SR<sub>25</sub>, S(O)<sub>p</sub>R<sub>26</sub>, C(=O)R<sub>25</sub>, OC(=O)R<sub>25</sub>, CO<sub>2</sub>R<sub>25</sub>, C(=O)NR<sub>25</sub>R<sub>26</sub>, NR<sub>25</sub>C(=O)R<sub>26</sub>, OC(=O)NR<sub>25</sub>R<sub>26</sub>, NR<sub>25</sub>CO<sub>2</sub>R<sub>26</sub>, NR<sub>27</sub>C(=O)NR<sub>25</sub>R<sub>26</sub> or NR<sub>25</sub>SO<sub>2</sub>R<sub>26</sub>; or R<sub>5a</sub> and R<sub>5b</sub>, R<sub>6a</sub> and R<sub>6b</sub>, or R<sub>8</sub> and R<sub>9</sub> taken together form a keto group (=O) or a monocyclic or bicyclic cycloalkyl or heterocyclo joined in a spiro fashion to ring E, or alternatively, R<sub>5a</sub> and/or R<sub>5b</sub> together with R<sub>8</sub> and/or R<sub>9</sub>, or R<sub>6a</sub> and/or R<sub>6b</sub> together with R<sub>8</sub> and/or R<sub>9</sub>, are taken to form a fused carbocyclic, heterocyclic, or heteroaryl ring; provided that, when G is a C<sub>1-6</sub>alkyl substituted with OR<sub>17</sub>, CO<sub>2</sub>R<sub>18</sub>, or C(=O)NR<sub>18</sub>R<sub>19</sub>, then R<sub>5a</sub>, R<sub>5b</sub>, R<sub>6a</sub>, and R<sub>6b</sub> are hydrogen provided R<sub>8</sub> and R<sub>9</sub> are not both hydrogen;~~

R<sub>8</sub> and R<sub>9</sub> are selected independently from hydrogen, alkyl, -(CH<sub>2</sub>)<sub>j</sub>-C(=O)alkyl, -(CH<sub>2</sub>)<sub>j</sub>-phenyl, -(CH<sub>2</sub>)<sub>j</sub>-naphthyl, -(CH<sub>2</sub>)<sub>j</sub>-C<sub>4-7</sub>cycloalkyl, -(CH<sub>2</sub>)<sub>j</sub>-heterocyclo, and -(CH<sub>2</sub>)<sub>j</sub>-heteroaryl, provided R<sub>8</sub> and R<sub>9</sub> are not both hydrogen, or R<sub>8</sub> and R<sub>9</sub> together form a spirocycloalkyl or spiroheterocyclic ring; and

*j* is selected from 0, 1, 2 and 3.

R<sub>10</sub> is selected from hydrogen, alkyl, substituted alkyl, cycloalkyl, aryl, heteroaryl, and heterocyclo;

R<sub>11</sub> is hydrogen or C<sub>1-8</sub>alkyl;

R<sub>12</sub> is C<sub>1-8</sub>alkyl, substituted C<sub>1-8</sub>alkyl, or cycloalkyl;

R<sub>13</sub>, R<sub>14</sub>, R<sub>15</sub> and R<sub>16</sub> are selected independently of each other from hydrogen, alkyl, substituted alkyl, amino, alkylamino, hydroxy, alkoxy, aryl, cycloalkyl, heteroaryl, or heterocyclo, or R<sub>13</sub> and R<sub>14</sub>, or R<sub>15</sub> and R<sub>16</sub>, when attached to the same carbon atom, may join to form a spirocycloalkyl ring;

R<sub>17</sub> is alkyl, substituted alkyl, cycloalkyl, aryl, heterocyclo, or heteroaryl;

R<sub>18</sub>, R<sub>19</sub>, and R<sub>20</sub> are independently selected from hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, heteroaryl, cycloalkyl, heterocyclo, or C(=O)R<sub>28</sub>; or when G is NH(C=O)R<sub>19</sub>, R<sub>19</sub> may be a bond joined to W to define a heterocyclo ring; provided, however, that when y is at least one, W is imidazolyl, indolyl, -NR<sub>21</sub>R<sub>22</sub>, or -OR<sub>23</sub>, and G is -NR<sub>18</sub>C(=O)R<sub>19</sub>, then R<sub>19</sub> is not a C<sub>1</sub>-alkyl having the substituent -NR<sub>29</sub>R<sub>31</sub>;

R<sub>21</sub> and R<sub>22</sub> are selected from hydrogen, alkyl, and substituted alkyl;

R<sub>23</sub> and R<sub>24</sub> are independently hydrogen, alkyl, substituted alkyl, aryl, heteroaryl, heterocyclo, and cycloalkyl;

R<sub>25</sub>, R<sub>26</sub> and R<sub>27</sub> are independently hydrogen, alkyl, substituted alkyl, cycloalkyl, aryl, heterocyclo, or heteroaryl; or R<sub>25</sub> and R<sub>26</sub> may join together to form a heterocyclo or heteroaryl, except R<sub>26</sub> is not hydrogen when joined to a sulfonyl group as in -S(O)<sub>p</sub>R<sub>26</sub> or -NR<sub>25</sub>SO<sub>2</sub>R<sub>26</sub>;

R<sub>28</sub> is hydrogen, alkyl, or substituted alkyl;

R<sub>29</sub> and R<sub>31</sub> are selected from hydrogen, alkyl, haloalkyl, hydroxyalkyl, phenylalkyl, and alkoxyalkyl, or R<sub>29</sub> and R<sub>31</sub> taken together form a heterocyclo ring;

n is 0, 1, 2, 3 or 4;

p is 1, 2, or 3;

x is 0, 1, or 2;

y is 0, 1, 2, 3 or 4; and

z is 0, 1, or 2.

2. (Currently amended) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate, thereof, in which:

~~in which:~~

G is selected from:

- a)  ~~$-\text{CO}_2\text{R}_{18}, -\text{C}(=\text{O})\text{NR}_{18}\text{R}_{19}, -\text{NR}_{18}\text{C}(=\text{O})\text{R}_{19}$ , and  $-\text{SO}_2\text{R}_{17}$ ;~~
- b)  $\text{C}_{1-6}$ alkylene or  $\text{C}_{2-6}$ alkenylene joined to one of ~~cyano,  $-\text{OR}_{17}, -\text{C}(=\text{O})\text{R}_{18}, -\text{CO}_2\text{R}_{18}$ ,~~  
 ~~$-\text{C}(=\text{O})\text{NR}_{18}\text{R}_{19}, -\text{NR}_{18}\text{C}(=\text{O})\text{R}_{19}, -\text{NR}_{18}\text{CO}_2\text{R}_{19}, -\text{NR}_{18}\text{SO}_2\text{R}_{17}, -\text{SO}_2\text{R}_{17}$ , and~~  
 ~~$-\text{NR}_{20}\text{C}(=\text{O})\text{NR}_{18}\text{R}_{19}$ , and  $-\text{SR}_{18}$ ;~~
- c) ~~or when W is a group other than  $\text{NHR}_{22}$ , G also may be selected from optionally substituted pyrrolidinyl or piperidinyl;~~

$\text{R}_{17}$  is  $\text{C}_{1-4}$ alkyl,  $\text{C}_{5-6}$ cycloalkyl, phenyl, or benzyl;

$\text{R}_{18}$ ,  $\text{R}_{19}$ , and  $\text{R}_{20}$  are independently selected from hydrogen,  $\text{C}_{1-4}$ alkyl, phenyl, benzyl,  $\text{C}_{5-6}$ cycloalkyl,  $-\text{C}(=\text{O})\text{CH}_2(\text{phenyloxy})$ ,  $-\text{C}(=\text{O})\text{CH}_2(\text{benzyloxy})$ , imidazolyl, pyridyl, furyl, thienyl, or  $\text{C}_{1-4}$ alkyl or  $\text{C}_{2-4}$ alkenyl substituted with one of phenyl, pyridyl, furyl, cyclopentyl, cyclohexyl,  $\text{CO}_2\text{Me}$ , phenyloxy, or benzyloxy, wherein each ringed group of  $\text{R}_{18}$ ,  $\text{R}_{19}$ , and  $\text{R}_{20}$  in turn is optionally substituted with one to two  $\text{R}_{36}$ , and/or optionally has a benzene ring or five membered heterocyclo having two oxygen atoms fused thereto; and

$\text{R}_{36}$  is halogen, methoxy, nitro, phenyl, phenyloxy, or alkylamino.

3. (Currently amended) A compound according to claim 2, or a pharmaceutically-acceptable salt or hydrate, thereof, in which

G is  $-\text{NR}_{18}\text{C}(=\text{O})\text{R}_{19}$ ,

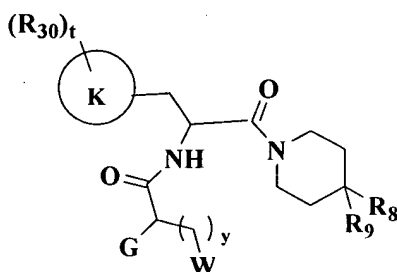
$\text{R}_{18}$  is hydrogen or lower alkyl, and

$\text{R}_{19}$  is  $\text{C}_{1-4}$ alkyl,  $\text{C}_{2-4}$ alkenyl, phenyl, benzyl,  $\text{C}_{5-6}$ cycloalkyl,  $-\text{C}(=\text{O})\text{CH}_2(\text{phenyloxy})$ ,  $-\text{C}(=\text{O})\text{CH}_2(\text{benzyloxy})$ , imidazolyl, pyridyl, furyl, thienyl, or  $\text{C}_{1-4}$ alkyl or  $\text{C}_{2-4}$ alkenyl substituted with one of phenyl, phenyl, pyridyl, furyl, cyclopentyl, cyclohexyl,  $\text{CO}_2\text{Me}$ , phenyloxy, and benzyloxy, wherein each ringed group of  $\text{R}_{19}$  in turn is optionally substituted with one to two  $\text{R}_{36}$ , and/or optionally has a benzene ring or five membered heterocyclo having two oxygen atoms fused thereto.

4. (Currently amended) A compound according to claim 2, or a pharmaceutically-acceptable salt or hydrate, thereof, in which W is  ~~$\text{OH}$ ,  $\text{NH}_2$ ,  $\text{NHalkyl}$ ,  $\text{N(alkyl)}_2$ , azetidiny, or imidazolyl;~~

~~piperidinyl, pyrrolidinyl, or  $\text{NHCO}_2(\text{alkyl})$ ; or a  $\text{C}_{4-7}$  cycloalkyl optionally substituted with lower alkyl,  $\text{NH}_2$ ,  $\text{NHalkyl}$ , or  $\text{N(alkyl)}_2$ .~~

5. (Previously presented) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate, thereof, having the formula:



in which

K is phenyl or thiazolyl;

$\text{R}_{30}$  is selected from  $\text{C}_{1-4}$ alkyl, hydroxy, alkoxy, halogen, nitro, cyano, amino, alkylamino, phenyl, and  $-\text{C}(=\text{O})\text{phenyl}$ ;

$t$  is 0, 1 or 2; and

$y$  is 0, 1 or 2.

6. (Currently amended) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate, thereof, in which

~~W is OH,  $\text{NR}_{21}\text{R}_{22}$ ,  $\text{NHC}(=\text{O})\text{R}_{24}$ , or  $\text{NHCO}_2\text{alkyl}$ ;~~

$\text{R}_{21}$  and  $\text{R}_{22}$  are independently selected from hydrogen,  $\text{C}_{1-8}$ alkyl, and  $(\text{CH}_2)_q\text{-J}$ , wherein J is selected from naphthyl, furanyl, indolyl, imidazolyl, pyrimidinyl, benzothienyl, pyridinyl, pyrrolyl, pyrrolidinyl, thienyl, and  $\text{C}_{3-7}$ cycloalkyl, wherein the alkyl, alkylene, and/or J groups of  $\text{R}_{21}$  and/or  $\text{R}_{22}$  are optionally substituted with up to three  $\text{R}_{33}$ ;

$\text{R}_{24}$  is selected from  $\text{C}_{1-6}$ alkyl, trifluoromethyl, alkoxyalkyl, furylalkyl, alkylaminoethyl, phenyl, pyrrolylalkyl, piperidinyl, and piperidinylalkyl, wherein  $\text{R}_{24}$  in turn is optionally substituted with one to two  $\text{C}_{1-4}$ alkyl and/or  $-\text{CO}_2(\text{C}_{1-4}\text{alkyl})$ ;

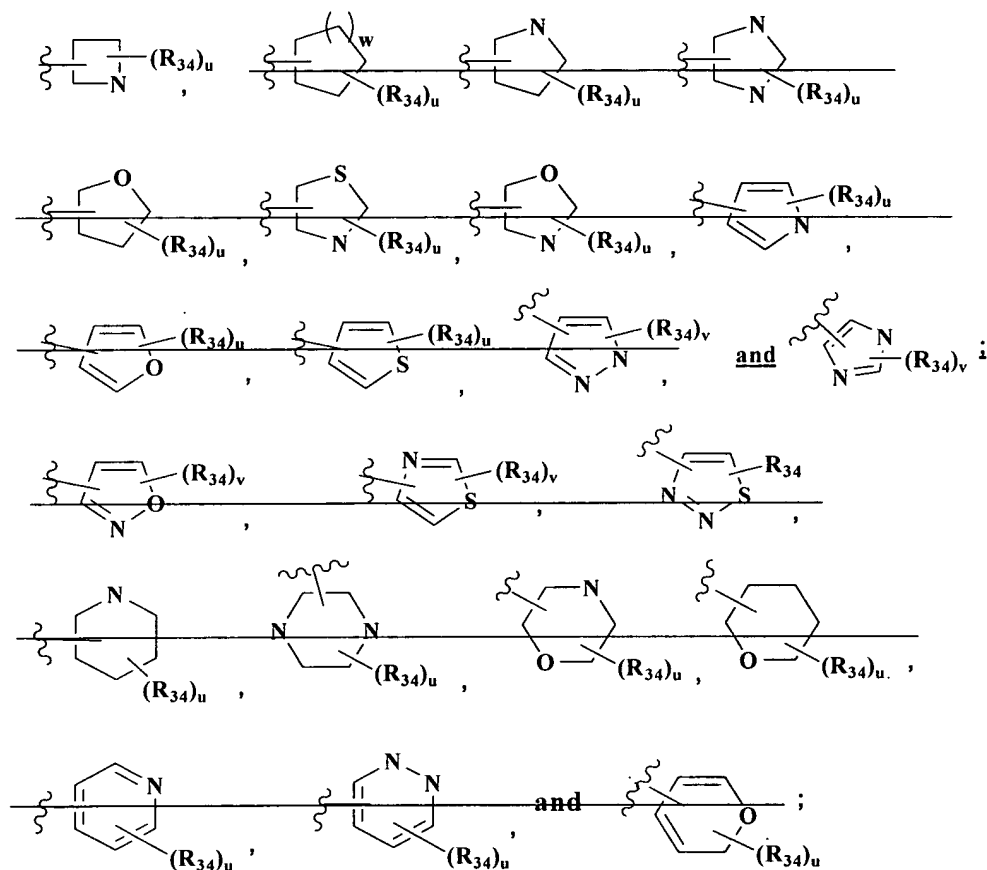
$\text{R}_{33}$  is selected from  $\text{C}_{1-6}$ alkyl, hydroxy,  $\text{C}_{1-4}$ alkoxy, amino,  $\text{C}_{1-4}$ alkylamino, amino $\text{C}_{1-4}$ alkyl, trifluoromethyl, halogen, phenyl, benzyl, phenyloxy, benzyloxy,  $-\text{C}(=\text{O})(\text{CH}_2)\text{NH}_2$ ,  $-\text{CO}_2(\text{C}_{1-4}\text{alkyl})$ ,  $-\text{SO}_2(\text{C}_{1-4}\text{alkyl})$ , tetrazolyl, piperidinyl, pyridinyl, and indolyl, wherein

when  $R_{33}$  includes a ring, said ring in turn is optionally substituted with one to two  $C_{1-4}$ alkyl, hydroxy, methoxy, and/or halogen; and

$q$  is 0, 1, 2 or 3.

7. (Currently amended) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate, thereof, in which

W is a ring selected from:



$R_{34}$  at each occurrence is attached to any available carbon or nitrogen atom of W and is selected from  $C_{1-6}$ alkyl, halogen, amino, aminoalkyl, alkylamino, hydroxy,  $C_{1-4}$ alkoxy, hydroxy $C_{1-4}$ alkyl,  $-C(=O)$ alkyl,  $-C(=O)$ aminoalkyl,  $-C(=O)$ phenyl,  $-C(=O)$ benzyl,  $-CO_2$ alkyl,  $-CO_2$ phenyl,  $-CO_2$ benzyl,  $-SO_2$ alkyl,  $-SO_2$ aminoalkyl,  $-SO_2$ phenyl,  $-SO_2$ benzyl, phenyl, benzyl, phenyloxy, benzyloxy, pyrrolyl, pyrazolyl, piperidinyl, pyridinyl, pyrimidinyl, and tetrazolyl, and/or two  $R_{34}$  when attached to two adjacent carbon atoms or adjacent carbon and nitrogen atoms may be taken together to form a fused benzo, heterocyclo, or heteroaryl ring, and/or

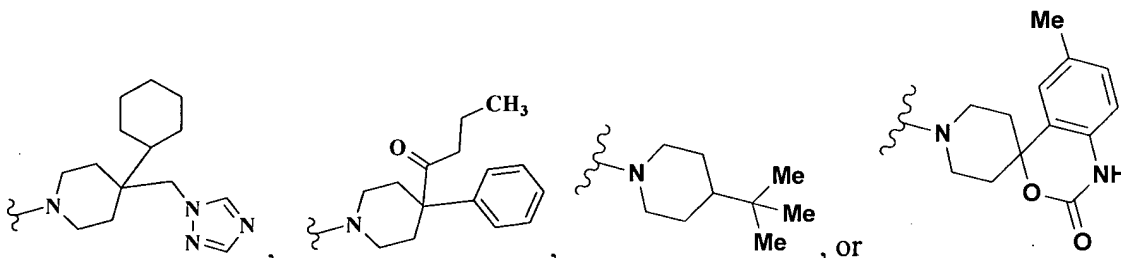
two R<sub>34</sub> when attached to the same carbon atom (in the case of a non-aromatic ring) may form keto (=O), and each R<sub>34</sub> in turn is optionally substituted with up to two R<sub>35</sub>; R<sub>35</sub> is selected from halogen, trifluoromethyl, C<sub>1-4</sub>alkyl, cyano, nitro, trifluoromethoxy, amino, alkylamino, aminoalkyl, hydroxy, and C<sub>1-4</sub>alkoxy; w is selected from 0, 1, or 2; u is selected from 0, 1, 2, and 3; and v is 0, 1 or 2.

8. (Previously presented) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate, thereof, in which

R<sub>8</sub> and R<sub>9</sub> are selected independently from hydrogen, alkyl, -(CH<sub>2</sub>)<sub>j</sub>-C(=O)alkyl, -(CH<sub>2</sub>)<sub>j</sub>-phenyl, -(CH<sub>2</sub>)<sub>j</sub>-naphthyl, -(CH<sub>2</sub>)<sub>j</sub>-C<sub>4-7</sub>cycloalkyl, -(CH<sub>2</sub>)<sub>j</sub>-heterocyclo, and -(CH<sub>2</sub>)<sub>j</sub>-heteroaryl, provided R<sub>8</sub> and R<sub>9</sub> are not both hydrogen, or R<sub>8</sub> and R<sub>9</sub> together form a spirocycloalkyl or spiroheterocyclic ring; and

j is selected from 0, 1, 2 and 3.

9. (Previously presented) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate, thereof, in which E is



10. (Previously presented) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate, thereof, in which

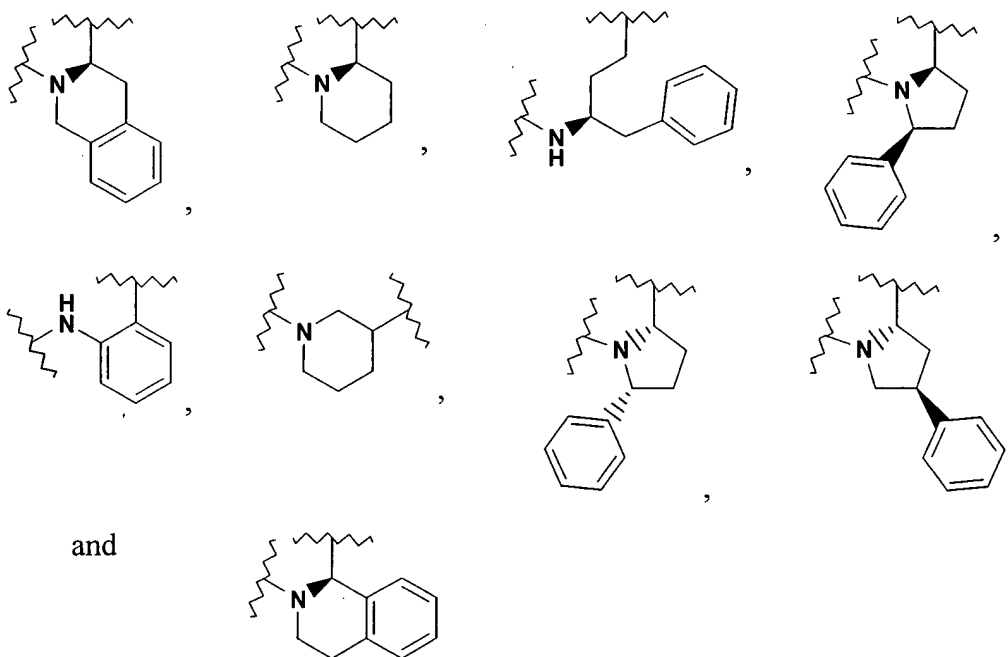
R<sub>2</sub> is selected from C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkenylene-K, and -(CH<sub>2</sub>)<sub>g</sub>-K;

K is selected from phenyl, naphthyl, thienyl, thiazolyl, pyridinyl, pyrimidinyl, and C<sub>5-6</sub>cycloalkyl, wherein each group K in turn is optionally substituted with one to three R<sub>30</sub> or has a benzene ring fused thereto, which also may be substituted with one to three R<sub>30</sub>;

R<sub>30</sub> is selected from C<sub>1-4</sub>alkyl, hydroxy, alkoxy, halogen, nitro, cyano, amino, alkylamino, phenyl, and acylphenyl; and

$g$  is 0, 1, 2 or 3.

11. (Currently amended) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate, thereof, in which  $\text{N(R}_1\text{)-CH(R}_2\text{)-}$   ~~$\text{X(R}_1\text{)-CH(R}_2\text{)-CH(R}_3\text{)-}$~~  $(\text{CH}_2)_g$ , taken together are selected from  $\text{C}_{1-4}$ alkylene,

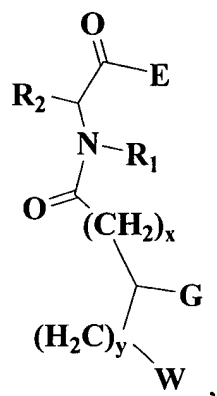


12. (Previously presented) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate, thereof, in which  $\text{R}_1$  is hydrogen or  $\text{C}_{1-4}$ alkyl.

13. (Canceled)

14. (Currently amended) A compound having the formula,

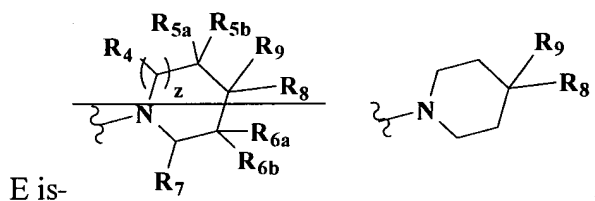




or a pharmaceutically-acceptable salt or hydrate, thereof, in which:

R<sub>1</sub> is hydrogen or C<sub>1-6</sub>alkyl or is taken together with R<sub>2</sub> or R<sub>3</sub> to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;

R<sub>2</sub> is C<sub>1-6</sub>alkyl or C<sub>2-6</sub>alkenyl optionally substituted with one to three-aryl, cycloalkyl, or heteroaryl, provided that where G is C<sub>2-6</sub>alkenyl, A<sub>1</sub>-NR<sub>18</sub>CO<sub>2</sub>R<sub>19</sub>, or A<sub>1</sub>-SO<sub>2</sub>R<sub>17</sub>, or when y is 0, R<sub>2</sub> may be or C<sub>1-6</sub>alkyl or C<sub>2-6</sub>alkenyl, each optionally substituted with heteroaryl;



G is selected from:

a) ~~CO<sub>2</sub>R<sub>18</sub>, C(=O)NR<sub>18</sub>R<sub>19</sub>, NR<sub>18</sub>C(=O)R<sub>19</sub>, and SO<sub>2</sub>R<sub>17</sub>;~~

b) C<sub>1-6</sub>alkylene or C<sub>2-6</sub>alkenylene joined to one of ~~cyano, OR<sub>17</sub>, C(=O)R<sub>18</sub>, CO<sub>2</sub>R<sub>18</sub>, C(=O)NR<sub>18</sub>R<sub>19</sub>, NR<sub>18</sub>C(=O)R<sub>19</sub>, NR<sub>18</sub>CO<sub>2</sub>R<sub>19</sub>, NR<sub>18</sub>SO<sub>2</sub>R<sub>17</sub>, SO<sub>2</sub>R<sub>17</sub>, and NR<sub>20</sub>C(=O)NR<sub>18</sub>R<sub>19</sub>, and SR<sub>18</sub>;~~

c) ~~or when W is a group other than NHR<sub>22</sub>, G also may be selected from optionally substituted pyrrolidinyl or piperidinyl;~~

W is selected from ~~NR<sub>21</sub>R<sub>22</sub>, OR<sub>23</sub>, NR<sub>21</sub>C(=O)R<sub>24</sub>, NR<sub>21</sub>CO<sub>2</sub>R<sub>24</sub>, amidino, guanidino, or a substituted or unsubstituted heterocyclo, heteroaryl, or cycloalkyl selected from azepinyl, azetidiny, and imidazolyl, imidazolidinyl, pyrazolyl, pyridyl, pyrazinyl, pyridazinyl, 1,2-dihydropyridazinyl, pyranyl, tetrahydropyranyl, piperazinyl, homopiperazinyl, pyrrolyl,~~

~~pyrrolidinyl, piperidinyl, thiazolyl, tetrahydrothiazolyl, thienyl, furyl, tetrahydrofuryl, morpholinyl, isoquinolinyl, tetrahydroisoquinolinyl, tetrazolyl, oxazolyl, tetrahydro-oxazolyl, and C<sub>3-7</sub>cycloalkyl~~, wherein said heteroaryl, heterocyclo or cycloalkyl groups may additionally have joined thereto an optionally substituted five-to-seven membered heterocyclic, heteroaryl, or carbocyclic ring;

~~R<sub>4</sub> and R<sub>7</sub> are independently selected from hydrogen, alkyl, substituted alkyl, halogen, hydroxy, alkoxy, and keto;~~

~~R<sub>5</sub>, R<sub>5a</sub>, R<sub>5b</sub>, R<sub>6</sub>, R<sub>6a</sub>, R<sub>6b</sub>, R<sub>8</sub> and R<sub>9</sub> are independently hydrogen, halogen, cyano, alkyl, substituted alkyl, alkenyl, hydroxy, alkoxy, alkoxycarbonyl, acyl, cycloalkyl, heterocyclo, aryl, or heteroaryl; or R<sub>5a</sub> and R<sub>5b</sub>, R<sub>6a</sub> and R<sub>6b</sub>, or R<sub>8</sub> and R<sub>9</sub> taken together form a keto group (=O) or a monocyclic or bicyclic cycloalkyl or heterocyclo joined in a spiro fashion to ring E, or alternatively, R<sub>5a</sub> and/or R<sub>5b</sub> together with R<sub>8</sub> and/or R<sub>9</sub>, or R<sub>6a</sub> and/or R<sub>6b</sub> together with R<sub>8</sub> and/or R<sub>9</sub>, join together to form a fused benzene or heterocyclo ring; provided that, when G is a C<sub>1-6</sub>alkyl substituted with OR<sub>17</sub>, CO<sub>2</sub>R<sub>18</sub>, or C(=O)NR<sub>18</sub>R<sub>19</sub>, then R<sub>5a</sub>, R<sub>5b</sub>, R<sub>6a</sub>, and R<sub>6b</sub> are hydrogen;~~

R<sub>8</sub> and R<sub>9</sub> are selected independently from hydrogen, alkyl, -(CH<sub>2</sub>)<sub>j</sub>-C(=O)alkyl, -(CH<sub>2</sub>)<sub>j</sub>-phenyl, -(CH<sub>2</sub>)<sub>j</sub>-naphthyl, -(CH<sub>2</sub>)<sub>j</sub>-C<sub>4-7</sub>cycloalkyl, -(CH<sub>2</sub>)<sub>j</sub>-heterocyclo, and -(CH<sub>2</sub>)<sub>j</sub>-heteroaryl, provided R<sub>8</sub> and R<sub>9</sub> are not both hydrogen, or R<sub>8</sub> and R<sub>9</sub> together form a spirocycloalkyl or spiroheterocyclic ring; and

*j* is selected from 0, 1, 2 and 3.

R<sub>10</sub> is selected from hydrogen, alkyl, substituted alkyl, cycloalkyl, aryl, heteroaryl, and heterocyclo;

R<sub>11</sub> is hydrogen or C<sub>1-8</sub>alkyl;

R<sub>12</sub> is C<sub>1-8</sub>alkyl, substituted C<sub>1-8</sub>alkyl, or cycloalkyl;

R<sub>17</sub> is alkyl, substituted alkyl, cycloalkyl, aryl, heterocyclo, or heteroaryl;

R<sub>18</sub>, R<sub>19</sub>, and R<sub>20</sub> are independently selected from hydrogen, alkyl, alkenyl, aryl, heteroaryl, cycloalkyl, heterocyclo, C(=O)R<sub>28</sub> or a C<sub>1-4</sub>alkyl or C<sub>2-4</sub>alkenyl substituted with one or more of aryl, heteroaryl, cycloalkyl, heterocyclo, alkoxycarbonyl, phenoxy, and/or benzyloxy, and each of said ringed groups of R<sub>18</sub>, R<sub>19</sub>, and R<sub>20</sub> in turn is optionally substituted with one to two R<sub>36</sub>;

R<sub>21</sub> and R<sub>22</sub> are selected from alkyl and substituted alkyl;

R<sub>23</sub> and R<sub>24</sub> are independently selected from hydrogen, alkyl, substituted alkyl, aryl, heteroaryl, heterocyclo, and cycloalkyl;

R<sub>28</sub> is hydrogen, alkyl, or substituted alkyl;

R<sub>36</sub> is halogen, methoxy, nitro, phenyl, phenoxy, or alkylamino;

n is 0, 1, 2, 3 or 4;

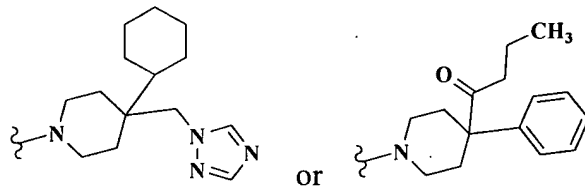
x is 0, 1, or 2;

y is 0, 1, 2, 3 or 4; and

z is 0, 1, or 2.

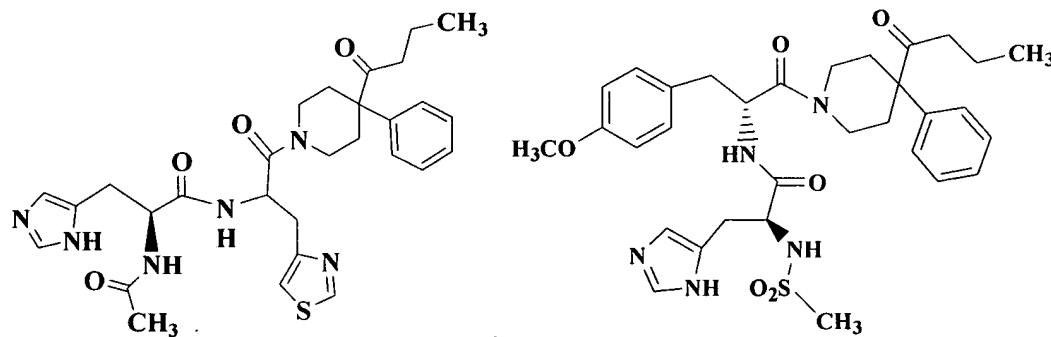
15. (Canceled)

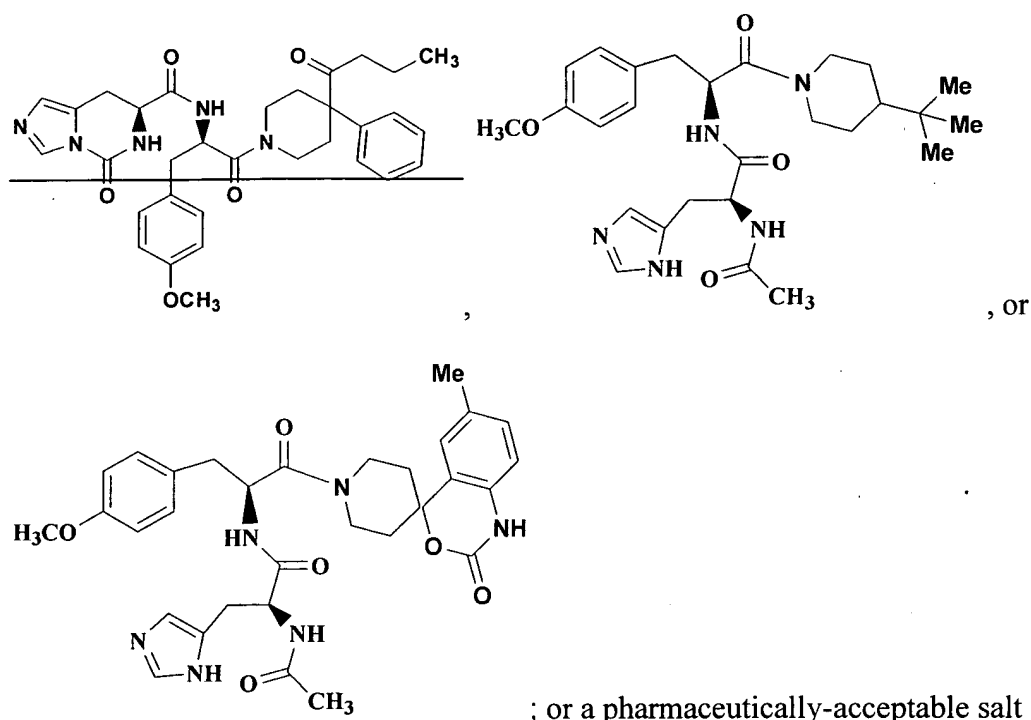
16. (Currently amended) A compound according to claim 14, or a pharmaceutically-acceptable salt or hydrate, thereof, in which E is



17. (Previously presented) A compound according to claim 14, or a pharmaceutically-acceptable salt or hydrate, thereof, in which G is NHC(=O)(alkyl) or NHC(=O)phenyl.

18. (Currently amended) A compound according to claim 1, having the formula,





19. (Previously presented) A pharmaceutical composition comprising at least one compound according to claim 1 or a pharmaceutically-acceptable salt or hydrate, thereof; and a pharmaceutically-acceptable carrier or diluent.
20. (Withdrawn) A pharmaceutical composition comprising (i) at least one compound according to claim 1 or a pharmaceutically-acceptable salt hydrate, or prodrug thereof; (ii) at least one second compound effective for treating an inflammatory or immune disease, a cardiovascular disease, or a neurodegenerative condition; and (iii) a pharmaceutically-acceptable carrier or diluent.
21. (Withdrawn) The pharmaceutical composition according to claim 20 in which the at least one second compound comprises a phosphodiesterase inhibitor.
22. (Withdrawn) A method of treating a melanocortin-receptor associated condition, the method comprising administering to a warm-blooded species in need of such treatment a therapeutically-effective amount of at least one compound according to claim 1.
23. (Withdrawn) The method of claim 22 in which the melanocortin-receptor associated condition is an MC-1R or MC-4R condition.